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DRUG THERAPY IN RESPIRATORY DISEASE¹

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In a specialized Medical Thoracic Unit, the greater proportion of patients presenting for treatment will be those who have what we call obstructive airways disease. This is a descriptive term, used to describe the physiological impairment which occurs in patients with asthma, emphysema, and/or chronic bronchitis.

It shall be my purpose here, therefore, to deal briefly with a group of drugs commonly used in the management of these patients and also, at times, in the pre-operative and post-operative management of thoracic surgical patients. Antibiotic therapy would be a subject in itself, and it is not proposed to discuss antibiotics at this stage, therefore, other than to briefly mention aerosol antibiotic therapy.

BRONCHODILATOR DRUGS

These drugs, when effective, do actively enlarge the lumen of bronchioles by effects on bronchiolar smooth muscle. However, with this initial increase in the size of the lumen, the patient will also be able more effectively to cough up secretions, and this, in turn, will further improve ventilation to the peripheral portions of the lung. Thus physiotherapy, and in particular postural drainage, will often be more successful if the patient is first given an effective bronchodilator drug.

Oral Therapy

The oral bronchodilators are relatively cheap and, in the patients with mild asthma, they may be very effective. However, they will be of limited value in the patient with severe or moderately severe asthma.

Ephedrine is the drug most commonly prescribed. Ephedrine may cause tremor, tachycardia, headache, and in elderly men it may precipitate urinary retention; it will need to be used with care in patients with cardiac disease.

In an attempt to reduce some of the side effects, ephedrine may be combined with a sedative, such as ephedrobarb, or with aminophylline and a sedative, e.g. Amesec, Theosec and Tedral.

Alupent (orciprenaline) and Neo-Epinephrine (isoprenaline) tablets are very closely related to ephedrine chemically and they have similar side effects. There will, therefore, be little to gain by giving more than one of these three drugs at the same time, as to do so would generally be of no greater therapeutic effect, but any side effects would be accentuated.

Aminophylline tablets fall into another class, however, and aminophylline may therefore be given in addition to a drug of the ephedrine group. Aminophylline tablets alone tend to be less effective than ephedrine. In

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addition, many patients will find they are unable to tolerate aminophylline because of nausea, vomiting, or abdominal discomfort. In an attempt to overcome this disadvantage, other aminophylline preparations have been developed but, like aminophylline itself, they may also be associated with gastric intolerance. Examples of such preparations are Cholelyl, Androphyllin, Elixophyllin and Quibron.

Parenteral Therapy

One of the most effective drugs available for the treatment of acute asthma is adrenaline. This drug is usually given subcutaneously and, in most cases, relief will be obtained in a matter of minutes. The side effects will be similar to those obtained with ephedrine but, because parenteral adrenaline is a more effective drug, it may on occasions be used where ephedrine has failed.

Where adrenaline has failed to provide sufficient relief, it is customary to proceed to parenteral aminophylline. This will be most effective if given intravenously. While a single injection may suffice, it will often be necessary to give the aminophylline by continuous intravenous drip. Often, a patient who has been unable to tolerate the drug orally, will experience no side effects whatsoever when the drug is given parenterally.

Aerosol Therapy

Aerosol therapy is now widely used in the management of patients with bronchial asthma. The therapeutic effect approaches that of parenteral adrenaline and yet, provided the dosage of the aerosol has been correctly determined, side effects will be few. This is due to the fact that a much smaller dosage of the drug will be required when the drug is administered in aerosol form.

If aerosol therapy is to be effective, however, a satisfactory nebuliser must be used. This should be capable of producing a mist composed mainly of particles one to three microns in size. Only small particles of this size will reach the smaller bronchioles, the larger particles being deposited progressively further up the air passages.

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It is not possible here to go into the different types of nebuliser currently available, but the drugs commonly used as aerosol bronchodilators are Neo-Epinine (isoprenaline) or Alupent (orciprenaline).

Where aerosol therapy has been prescribed, it is important that it be not used excessively by the patient. With regard to this, he must be guided by his own doctor.

EXPECTORANTS

Iodides and other expectorants have been used for many years, in the belief that they might change the character of the sputum by thinning the bronchial secretions. While many clinicians remain firmly convinced that iodides are of value, it is difficult to prove that they do, in fact, have any effect at all.

ENZYMES

Because enzymes can attack proteins and mucin and break them into simpler compounds, enzymes have been used in aerosol form in the treatment of pulmonary disease. Enzymes which have been used include crystalline trypsin, streptodornase, streptokinase, hyaluronidase, and lysozyme. Some of these enzymes have been available in this country under various trade names. However, the results have not been impressive and the side effects have been relatively high. Irritation of the eyes and of the respiratory tract and hypersensitivity reactions have been reported. For these reasons, the enzymes have found little place in the clinical management of patients.

OTHER MUCOLYTIC AGENTS

Mucomyst (acetylcysteine)

In recent years, many favourable reports have appeared concerning this drug. It is claimed that it reduces the viscosity of mucus to a greater extent than do saline solutions, proteolytic enzymes, or detergents. This is said to apply to both purulent and non-purulent bronchial secretions. Although this would appear to be the most promising drug available within this group at present, further evaluation will be needed.

Mucomyst is given in aerosol form and details concerning dosage and administration are provided with the drug.

Side effects have not been common, but a few cases of stomatitis, nausea, and occasional rhinorrhea have been reported. The drug must be used with care in patients with bronchial asthma, as it may aggravate "bronchospasm". If the latter should occur, the patient must immediately be given a bronchodilator drug.

Ascoxal

Ascoxal is made up of ascorbic acid, sodium percarbonate, and copper sulphate. Made up as an aerosol, it has been claimed to be an effective mucolytic agent. However, there is as yet little evidence to support this claim.

DETERGENTS

Alevaire is available in a sterile aqueous solution for aerosol use, containing a detergent, superinone, with sodium bicarbonate and glycerine. It is considered by some that sputum might more easily be mobilized by use of a detergent such as superinone. While the drug is apparently non-toxic, recent reports would suggest that Alevaire delivered by aerosol is, in fact, no more effective than simple humidification.

AEROSOL ANTIBIOTIC THERAPY

In most cases, patients with chronic bronchial infection will respond satisfactorily to systemic antibiotic therapy. On occasions, however, where purulent sputum remains in spite of intensive therapy by conventional methods, an aerosol antibiotic may be tried. It is usual here to use only antibiotics which the patient is not likely to require, either orally or parenterally, in the future.

The antibiotics which are more commonly used in this way are Neomycin, Polymyxin and Kanamycin.

Unfortunately, where systemic antibiotic therapy has failed, the results of aerosol therapy with these drugs will often be disappointing.

STEROID DRUGS

Included under this heading will be cortisone, hydro-cortisone, and derivatives such as prednisone, prednisolone, triamcinolone, betamethasone, and methyl-prednisolone. Some of these drugs will be better known by their trade names — triamcinolone (Leder-cort), betamethasone (Celestone, Betnelan).

In patients with severe bronchial asthma or related conditions, steroid drugs will, on occasions, be required as a life-saving measure. Under these circumstances, it may be possible to stop the drug within a few weeks of its commencement. There are, however, a large group of patients in whom respiratory disability has progressed to the stage where they are no longer able to continue their work, and may have even become completely bedridden. In some of these cases, steroid drugs will be employed. However, a very thorough assessment, preferably with the aid of pulmonary function tests, should be made before a patient is committed to long term steroid therapy. The risks of steroid therapy are not insignificant, but where other drugs have proved ineffective, their use will, on occasions, be warranted.

SUMMARY

In patients with airways obstruction due, in particular, to asthma or chronic bronchitis, steroid drugs will, on occasions, be required, but the routine bronchodilator drugs, in particular the aerosol bronchodilators, will in general be most effective.

Where bronchodilator therapy has been prescribed for a patient who is also having physiotherapy, the patient will often be able to manage the latter more easily if the bronchodilator drug has been given initially.

If only an oral bronchodilator has been used, then this should be taken half an hour to an hour before the physiotherapy; whereas if the drug is to be given by aerosol or parenterally, then the interval between the drug and the physiotherapy would need to be only five to ten minutes.

On occasions, where the patient continues to have difficulty in coughing up thick secretions, in spite of antibiotic and broncho-

dilator therapy, a mucolytic agent such as Mucomyst may be tried. Detergents such as superinone, on the other hand, would appear to have no therapeutic effect over and above that produced by use of a suitable humidifier.

Expectorants such as potassium iodide orally continue to be used, but no objective evidence has been produced to show that the use of iodides does in any way affect the nature of the bronchial secretions.